Claim Rejection under U.S.C. § 112, First Paragraph

The Examiner rejects claims 1, 3, 4, and 7-13 as allegedly failing to comply with the written description requirement. Specifically, the Office Action asserts that the previous introduction of "only one signature motif B^1XXLL" into the claims allegedly resulted in the introduction of new matter due to the consolidation of the subject matter of canceled claim 23 into claim 1. The Examiner contends that the support for claim 1 and certain dependant claims, does not present a working example of the claimed invention. The Examiner concedes that working example 6 teaches an *in vitro* binding assay that includes SRC-1 protein, but alleges inclusion of more than one LXXLL motif in the inhibition assay. The Examiner further asserts that even in the event that only one LXXLL motif or mutant form thereof was used in Example 6, this would still not provide support for the full scope of claim 1. Applicants respectfully traverse this rejection.

Applicants reiterate the arguments already made of record and contend that one of skill in the art could readily envision the claimed matter in view of the teachings of the specification. The description of the invention describes the use of "a nuclear protein fragment comprising a signature motif of the nuclear protein," where the use of "a" includes "only one signature motif." The description of the nuclear protein fragment includes the following statement: "a preferred fragment size of a nuclear protein is 8-10 amino acids." The length of this very short fragment allows for 1, or at most 2 of the 5 amino acid signature motifs within a given fragment. The depiction of the utility of the receptor protein fragments in Figures 1a and Figure 2b clearly shows peptides containing only one signature motif in the binding assays with liganded nuclear receptors. Accordingly, the specification plainly includes explicit support for the use of fragments including only one signature motif in the claimed assays, contrary to the Examiner's assertions.

Furthermore, even if the specification lacked any explicit teachings of fragments including only a single signature motif, Applicants are entitled to claim less than the full scope of their invention, which even the Examiner admits includes fragments comprising one or more signature motifs. For example, in *In re Wertheim*, 541 F.2d 257 (C.C.P.A. 1976), the court's analysis of a claimed invention that encompasses less than the full scope of the invention as described in the specification is instructive:

> The function of the description requirement is to ensure that the inventor had possession, as of the filing date of the application relied on, of the specific subject matter

later claimed by him; how the specification accomplishes this is not material.... It is not necessary that the application describe the claim limitations exactly, ... but only so clearly that persons of ordinary skill in the art will recognize from the disclosure that appellants invented processes including those limitations. [citations omitted]

The primary consideration is factual and depends on the nature of the invention and the amount of knowledge imparted to those skilled in the art by the disclosure.

...

That what appellants claim as patentable to them is less than what they describe as their invention is not conclusive if their specification also reasonably describes that which they do claim. Inventions are constantly made which turn out not to be patentable, and applicants frequently discover during the course of prosecution that only a part of what they invented and originally claimed is patentable. As we said in a different context in *In re Saunders*, 58 CCPA 1316, 1327, 444 F.2d 599, 607, 170 USPQ 213, 220 (1971):

> 'To rule otherwise would let form triumph over substance, substantially eliminating the right of an applicant to retreat to an otherwise patentable species merely because he erroneously thought he was first with the genus when he filed.' (541 F.2d at 262-263)

In another case raising similar issues, *In re Johnson*, 558 F.2d 1008 (C.C.P.A. 1977), the applicant sought to exclude two species which were lost in an interference proceeding from the scope of the claims. The Examiner contended that the amendments were not supported by the original application; however, upon appeal, the examiner's ruling was overturned.

> The notion that one who fully discloses, and teaches those skilled in the art how to make and use, a genus and numerous species there within, has somehow failed to disclose, and teach those skilled in the art how to make and use, that genus minus two of those species, and has thus failed to satisfy the requirements of § 112, first paragraph, appears to result from a hypertechnical application of legalistic prose relating to that provision of the statute. All that happened here is that appellants narrowed their claims to avoid having them read on a lost interference count.
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> ... Here, as we hold on the facts of this case, the "written description" ... supported the claims in the absence of the limitation, and that specification, having described the whole, necessarily described the part remaining. The facts of the prosecution are properly presented and relied on, under these circumstances, to indicate that appellants are merely excising the invention of another, to which they are not entitled, and are not creating an "artificial subgenus" or claiming "new matter." (at 1019)

A third case in support of Applicants' amendment to narrow the scope of the claims, *In re Patrick R. Driscoll* 562 F.2d 1245; 1977 CCPA LEXIS 110; 195 U.S.P.Q. (BNA) 434 (C.C.P.A. 1977), further demonstrates that narrowing amendments of the sort sought by Applicants are entirely permissible under the written description requirement. In that case, the applicant's attempt to narrow the definition of a substituent R group from a Markush group of fourteen variable substituents to only one member of the original group, an alkylsulfonyl moiety (C1-C6), was rejected under examination. Upon appeal of the rejected claim, the court found that a skilled artisan would recognize that the Markush claim reciting fourteen distinct substituents included the alkylsulfonyl substituent of the narrowed claim and that to rule otherwise would set a precedent resulting in a proliferation of claims attempting to cover all possible individual R variants.

> This record presents yet another instance of the sort of "hypertechnical application" of the written description requirement of §112 which was recently criticized in *In re Johnson*, F.2d, 194 USPQ 187 (CCPA 1977). Were the board's decision permitted to stand, future applicants, particularly in cases of this nature, would in all likelihood find themselves in the predicament reflected in the following observation by Judge Learned Hand:
>
> > "If, when [applicants] yield any part of what they originally believed to be their due, they substitute a new 'invention,' only two courses will be open to them: they must at the outset either prophetically divine what the art contains, or they must lay down a barrage of claims, starting with the widest and proceeding by the successive incorporation of more and more detail, until all combinations have been exhausted which can by any possibility succeed. The first is an impossible task; the second is a custom already more honored in the breach than in the observance, and its extension would only increase that surfeit of verbiage which has for long been the curse of patent practice, and has done much to discredit it. It is impossible to imagine any public purpose which it could serve." (at 1248)

Accordingly, it is clear that Applicants' pending claims are fully compliant with the written description requirement, following applicable legal precedent and patent policy as detailed above. In contrast, the present rejection is nothing more than another instance of a "hypertechnical application" of the written description requirement. Accordingly, the rejection on this basis should be withdrawn.

In regard to the enablement of the rejected claims, Applicants have provided working examples (Examples 1 and 2), in which 15 of 17 nuclear protein fragments containing only one LXXLL motif and a DNA binding domain (DBD) display ligand-dependant interaction with the LBD of the estrogen receptor (ER) whereas the DBD alone showed no ability to bind. Applicants have also provided in Example 6 an *in vitro* binding assay with an SRC-1 protein and a single motif peptide fragment to a liganded nuclear receptor (GST-AF2). In Figure 2b, the presence of a 14 amino acid peptide fragment with only one LQQLL motif blocks SRC-1a, a protein which contains multiple LXXLL binding motifs, from binding to the nuclear receptor while a mutant peptide does not inhibit SRC-1a binding. In light of these examples, it is unquestionable that a fragment (e.g., a first region as recited in claim 1) containing only a single binding motif can interact with a second region as recited in claim 1, and that interference with this interaction by a potential inhibitor compound can be detected just as it would be for a fragment with multiple binding motifs. Certainly, the Office Action offers neither factual evidence nor logical analysis to the contrary. Accordingly, the claimed "method for identifying an inhibitor compound...wherein the fragment comprises only one signature motif," is clearly enabled without the need for undue experimentation. Reconsideration and withdrawal of this rejection are respectfully requested.

Claim Rejections under 35 U.S.C. § 103(a), First Paragraph

The Office Action rejects claims 1, 7, 9, and 12 as allegedly being unpatentable over Lee et al. in view of Onate et al. The Examiner specifically points out that Lee et al. teach a binding assay of TRIP-1, which contains an MLELL motif, with a liganded nuclear thyroid hormone receptor transcription factor. The Examiner alleges that in view of the SRC-1 studies performed by Onate and co-workers, wherein SRC-1 is identified as a transcription coactivator, the current claims are anticipated. Applicants respectfully traverse these grounds for rejection.

Applicants submit that while Lee at al. teach an interaction between a peptide containing a single MXXLL motif and a thyroid hormone receptor, the authors do not teach or suggest that this motif is the binding domain or a domain of any significance in the TRIP-1 sequence. It would not be deduced from this study that any specific sequence within the 406 TRIP-1 amino acid sequence: a) is responsible for liganded nuclear receptor binding or transcriptional regulation; b) is conserved among coactivator proteins; or c) could be used to identify a nuclear receptor inhibitor. Lee makes no mention of the SRC-1 nuclear protein of the current application.

The Examiner has alleged that the methods of Lee at al. with the TRIP-1 protein could be extended to the coactivator SRC-1, the subject of Onate et al., rendering the presently claimed invention an obvious extension of the two methods. However, according to Onate et al., pursuit of homology studies with SRC-1 and known coactivator proteins would be envisaged as an *unproductive* pathway.

> "Multiple factors have been demonstrated to interact with steroid receptors in a ligand-dependent manner. These include a mouse bromodomain-containing protein, TIP1 (13), the human homolog of the adaptor Sug1p; TRIP1 (14) and other thyroid hormone receptor-interacting proteins (Trips) (15); and the ER-associated proteins ERAP160 (16), RIP160, and RIP80 (17).
>
> ...
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> However none of these proteins has been shown to enhance receptor-mediated transcriptional activity; therefore, their role as potential coactivators has yet to be defined. Recently, Cavailles et al (18) identified RIP140 as a potential coactivator for ER. However, sequence alignment at the amino acid level reveals no significant homology between these two proteins. In addition, RIP140 has only a modest effect on ER transactivation. SRC-1 also shares no significant homology to either TIF1 or TRIP1, nor does it contain similar functional canonical domains. Therefore, it is likely that the mechanism by which SRC-1 alters the rate of transcription will differ." (emphasis added)

Applicants submit that the underlined portion of the text indicates that there is no motivation to apply the TRIP-1 methods to SRC-1, and that there would be no reasonable expectation of success even if the combination were made. In fact, the passage actually *teaches away* from the claimed invention by suggesting that interchangeability is in fact *unlikely*. Onate concedes that the mechanism by which the coactivators function with nuclear proteins is unclear, further distancing the combination from any reasonable expectation of success:

> "Although we cannot rule out potential effects on chromatin structure, our evidence indicates that SRC-1 acts by direct contact with the receptor protein to modulate its activity. This interaction is likely to be a key regulatory event in the multiple-step steroid receptor transactivation pathway that occurs in vivo. Identification of several proteins with potential roles in steroid receptor action indicates that the activation process for steroid receptors is exceedingly complex and that the ultimate mechanism by which these factors act to modulate the transcription of specific gene networks remains to be elucidated." (emphasis added)

Applicants submit that the underlined text in the preceding passage underscores the inventiveness of the recognition of the importance and function of the signature motif recited in the present claims to explain a common mechanism amongst this structurally diverse set of proteins. Accordingly, for the foregoing reasons, Applicants submit that a *prima facie* case of obviousness has not been made out on the basis of the cited references. Reconsideration and withdrawal of this rejection are respectfully requested.

CONCLUSION

In view of the above remarks, Applicants believe that the pending application is in condition for allowance. Early and favorable reconsideration is respectfully solicited.

Applicants believe that no other fee is due with this response. However, if a an additional fee is due, please charge our Deposit Account No. 18-1945, under Order No. ASZD-P01-228 from which the undersigned is authorized to draw.

Dated: February 8, 2007

Respectfully submitted,

By _____

David P. Halstead
Registration No.: 44,735
FISH & NEAVE IP GROUP, ROPES & GRAY LLP
One International Place
Boston, Massachusetts 02110-2624
(617) 951-7000
(617) 951-7050 (Fax)
Attorneys/Agents For Applicant